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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,913	01/05/2006	Paul William Manley	ON/4-32700A	6405

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
07/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,913	MANLEY ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on April 3, 2008.

Claims 1-8 and 11 are pending in this application.

Withdrawn Rejections/Objections:

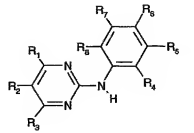
Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

Claims 1-8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buerger et al., WO 02/22597. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive.

As indicated in the previous office action, the reference teaches substituted pyrimidine compounds of formula (I):



(I),

wherein:

R_1 is unsubstituted pyridyl;

R_2 and R_3 are hydrogen;

one of R_4, R_5, R_6, R_7 and R_8 is a group of formula (II): $-N(R_9)-C(=X)-(Y)_n-R_{10}$

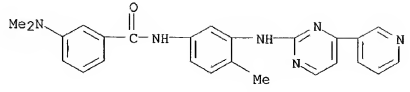
wherein R_9 is H, X is O, n is **0** and

R_{10} is phenyl which is

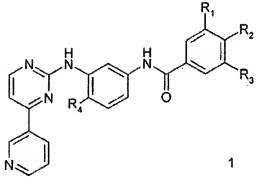
a) substituted by a radical selected from the group consisting of amino; mono- or di-lower alkylamino; lower alkanoylamino; formyl; lower alkoxy-carbonyl; and lower alkyl which is substituted by amino, mono- or di-lower alkylamino or lower alkanoylamino, or b) substituted by an unsubstituted or substituted radical selected from the group consisting of benzylamino; benzoylamino; pyrrolidinyl; piperidyl; piperazinyl; piperazinyl-carbonyl; morpholinyl; and lower alkyl substituted by benzylamino, benzoylamino, pyrrolidinyl, piperidyl, piperazinyl or morpholinyl, the substituents of said substituted radical being selected from the group consisting of cyano; lower alkyl; hydroxy- or amino-substituted lower alkyl; trifluoromethyl; hydroxy; lower alkoxy; lower alkanoyloxy; amino; mono- or di-lower alkylamino; lower alkanoylamino; benzoylamino; carboxy; lower alkoxycarbonyl and halogen, and c) optionally further substituted by one or more radicals selected from the group consisting of cyano; lower alkyl; hydroxy- or amino-substituted lower alkyl; trifluoromethyl; hydroxy; lower alkoxy; lower alkanoyloxy; amino; mono- or di-lower alkylamino; lower alkanoylamino; benzoylamino; carboxy; lower alkoxycarbonyl and halogen,

As can be seen from the above, the reference teaches that the phenyl ring represented by R_{10} is substituted by a substituent as described in option (a) or option (b) **and** further optionally substituted by additional substituent as described in option (c) selected from the group consisting of lower alkyl, trifluoromethyl, etc.

The reference further discloses several specific compounds falling within the above genus, see for example, the compound of Example 11:



The instant claims recite a genus of formula 1 (depicted below for convenience):



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wherein R_4 can be methyl; one of R_1 and R_2 is NR_5R_6, wherein R_5 and R_6 are selected from hydrogen, alkyl, etc. and the other is hydrogen; R_3 is alkyl, etc. As can be seen from the above, the instantly claimed compounds differ from the reference disclosed compound of Example 11, by having an additional substituent on the terminal phenyl ring. The reference, however, teaches that the phenyl ring may be additionally substituted by any of the substituents listed in option (c) which include alkyl, trifluoromethyl, etc. The reference compounds are taught to be useful as pharmaceutical agents having tyrosine kinase inhibitory activity. One of ordinary skill in the art would have been motivated to modify the reference disclosed compound by having an additional substituent listed in option (c), for example, a methyl group, with the reasonable expectation of obtaining compounds having same activity and therefore, the same utility as taught for the

reference compound. One of ordinary skill in the art in possession of the reference disclosed compounds, for example the compound of Example 11, with the disclosed therapeutic activity would have immediately recognized that a single change in substitution such as replacing the hydrogen with a methyl group on the pyrimidinyl ring can be done without the loss of the pharmacological activity. A single change in substitution of the reference disclosed compound would have resulted in a compound falling within the claimed structural formula 1 wherein the terminal phenyl ring carries two substituents. The reference, however, teaches that the phenyl may be additionally substituted with the substituents listed in option (c). Accordingly, the reference contains sufficient teaching of the molecular modifications required to prepare the instantly claimed compounds.

Applicant's citation of *Takeda v. Alphapharm* is acknowledged. The rebuttal argument based on *Takeda* case is not persuasive because the situation is *Takeda* is different from the instant case. The court in that case ruled that 'one of ordinary skill in the art would not have been prompted to modify the reference compound, using the steps of homologation **and** ring-walking, to synthesize the claimed compounds'. Contrary to the cited *Takeda* ruling, in the instant application, one of ordinary skill in the art needs to modify the reference disclosed specific compound by substituting an additional substituent, which is listed as an optional substituent for the phenyl ring, to arrive at the instantly claimed compound represented by formula 1.

Applicant argues that 'the presently claimed compounds have shown unexpected results in that the claimed compounds have in vitro IC50 values for Bcr-Abl as low as 10nM'. This is not persuasive because the reference teaches a biological activity for the disclosed compounds, i.e., as tyrosine kinase inhibitors, which is sufficient to one of ordinary skill to make the claimed

compounds because similar activity or properties are normally presumed when compounds are very close in structure. There is nothing on the record to show that the reference compounds did not possess the activity disclosed for the instant compounds. Applicants must prove that their compounds possess a property that the prior art compounds do not possess. If the prior art compound does in fact possess a particular activity or benefit, even though the activity or benefit is not recognized in the prior art, applicant's recognition of the activity or benefit is not in itself sufficient to distinguish the claimed compounds from the prior art. See *In re Best*, 195 USPQ 430 (CCPA 1977).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

July 27, 2008